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Retrospective Study

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Retrospective comparison of early- versus late-insulin therapy regarding effect on time to resolution of diabetic ketosis and ketoacidosis in dogs and cats: 60 cases (2003–2013)

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Abstract

Objective – To determine whether early insulin administration (≤6 h after admission) results in more rapid resolution of diabetic ketosis (DK) and ketoacidosis (DKA), shorter duration of hospitalization, and higher incidence of complications, and whether more severe ketonuria is associated with longer time to resolution of DK/DKA.
Design – Retrospective study (January 1, 2003–March 1, 2013).
Setting – University teaching hospital.
Animals – Sixty dogs and cats with DK or DKA receiving short-acting insulin therapy.
Interventions – None.
Measurements and Main Results – Medical records were reviewed and data recorded including signalment; previous history of diabetes; intake temperature, blood pressure, blood glucose, pH, base excess, and degree of ketonuria; time to short-acting insulin therapy and resolution of DK/DKA; length of hospitalization; and complications. Insulin was initiated ≤6 hours in the early group and >6 hours in the late group after hospital admission. Early group patients had more rapid resolution of DK/DKA after starting short-acting insulin therapy (36.4 ± 22.6 vs. 55.4 ± 26.6 h, $P = 0.014$). There was no difference in duration of hospitalization or complications. More severe ketonuria resulted in longer time to resolution of DK/DKA after initiation of short-acting insulin (severe: 50.9 ± 24.2; moderate: 29.6 ± 19; mild: 23.4 ± 21.9 h, $P = 0.005$, all individual pairwise comparisons $P < 0.05$).
Conclusions – Early insulin administration is associated with more rapid resolution of DK/DKA without an associated increase in complication rates. DK/DKA took longer to resolve with more severe ketonuria. Prospective studies are warranted to identify specific time targets for insulin administration in DK/DKA patients.

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Keywords: DKA, glucosuria, hyperglycemia, ketonemia, ketonuria, metabolic acidosis

Introduction

Diabetic ketosis (DK) and ketoacidosis (DKA) are severe, potentially life-threatening complications of diabetes mellitus that are characterized by hyperglycemia, glucosuria, and ketonemia or ketonuria; DKA also results in metabolic acidosis.[1–5] Treatment of DK/DKA focuses on appropriate IV fluid resuscitation, management of electrolyte derangements, insulin therapy, and targeted therapy for comorbid conditions.[1] The optimal

Abbreviations

BG	blood glucose concentration
CE	cerebral edema
CRI	continuous rate infusion
DK	diabetic ketosis
DKA	diabetic ketoacidosis
KB	ketone body

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timing for instituting short-acting insulin therapy is unclear from the veterinary literature and recommendations for timing of insulin initiation have largely been based on expert opinion rather than evidence.[2,6,7]

Justification for delaying insulin administration stems predominantly from the idea that blood glucose concentration (BG) decreases somewhat with fluid therapy alone, combined with concern about the development of metabolic complications from insulin therapy. Fluid therapy decreases BG because fluids reduce insulin resistance by decreasing concentrations of counterregulatory hormones, increase insulin availability to peripheral tissues, dilute the BG, and increase glomerular filtration rate, thereby increasing urinary glucose loss.[3,8–13] This reduction in BG has historically been thought to cause a significant decrease in effective osmolality, theoretically leading to dangerous complications such as cerebral edema (CE).[8] Despite the fact that CE remains a concern in the management of DKA, particularly in human children, studies have demonstrated that decline in BG bears little consequence on the development of CE.[14] Instead, studies have shown that inadequate normalization of serum sodium concentration with declining BG bears greater impact on effective osmolality and potential for neurologic complications.[15,16] Recent studies in veterinary medicine have demonstrated that measured serum osmolality does not correlate with BG in dogs and cats with DK and DKA, and is more closely associated with changes in serum sodium concentration, suggesting that the concern over rate of BG normalization is unwarranted.[17,18]

Clinically significant electrolyte disturbances are also common during DK and DKA, and these derangements can be exacerbated by insulin therapy.[3,5,9,19,20] Therefore, in order to minimize complications, it has been recommended to delay insulin therapy until patients are volume resuscitated and clinically significant electrolyte derangements are corrected.[13] In practice, some veterinarians delay insulin therapy until patients are rehydrated and central venous catheters are placed for blood sampling.[2]

Ultimately, however, insulin is required to stop ketogenesis, increase ketone body (KB) metabolism, decrease gluconeogenesis, and promote glucose utilization.[13] Because exogenous insulin therapy is required for resolution of DK/DKA, some recommend earlier insulin administration. In people, the recommendation is to initiate insulin therapy after the first hour of volume resuscitation, pending a serum potassium concentration $\geq$3.3 mmol/L.[21]

The effect of the timing of insulin administration on outcome has not been previously reported in veterinary medicine. We hypothesized that earlier administration of insulin therapy in dogs and cats would be associated with more rapid resolution of DK/DKA status and shorter hospital stays. Additionally, we hypothesized that there would be no difference in complications associated with insulin administration between early- and late-initiation insulin therapy. Finally, we hypothesized that more severe ketonuria at presentation would be associated with slower resolution of DK/DKA.

Materials and Methods

Dogs and cats admitted to a university teaching hospital between the years 2003 and 2013 with a diagnosis of DK or DKA were considered for inclusion. The diagnosis of DK or DKA was made if the patient was hyperglycemic with BG >13.9 mmol/L (250 mg/dL) or was euglycemic on admission with a history of diagnosed diabetes mellitus being treated with long-acting insulin administration, and had ketonuria based on detection with nitroprusside strips. Acidemia was not a requirement for inclusion and animals with DK and DKA were assessed collectively. Treatment with either intravenous continuous rate infusion (CRI) or intermittent IM or SQ short-acting insulin was also an inclusion criterion. Animals with multiple visits for DK/DKA management during the study period were included in the analyses with each hospitalization event treated as a separate case.

Animals were excluded from data analysis if they died or were euthanized prior to administration of insulin therapy, had long-acting insulin initiated prior to the resolution of DK/DKA, had ketonemia alone without concurrent ketonuria (because resolution of ketonuria was used as the criterion for resolution of an animal's DK or DKA status), or had unavailable or missing medical records. If specific data points were unavailable from individual patients, these cases were not included in the analysis.

Data were collected retrospectively, and included the patient's signalment and whether or not there was a preexisting diagnosis of diabetes mellitus being treated with long-acting insulin therapy. Presentation physical examination findings and blood pressure were recorded. Hypothermia was defined as a rectal temperature <37.9°C (100.2°F) in dogs and <38.1°C (100.5°F) in cats.[22] Hypotension was defined as a systolic arterial blood pressure <90 mm Hg or a mean arterial blood pressure <60 mm Hg assessed indirectly by Doppler or oscillometric technique.[23]

Presentation pH, base excess, and BG as determined using a blood gas analyzer[a] were recorded. Presentation urine KB concentration assessed using colorimetric, semiquantitative reagent strips[b] was also noted. Animals were classified as having mild, moderate, or severe ketonuria based on the results of these test strips. BGs were assessed every 2 hours over the course of

hospitalization using a glucometer[c] or the blood gas analyzer. Electrolytes and acid–base status were assessed at the discretion of the attending clinician using the blood gas analyzer or a blood chemistry analyzer. Serum magnesium and phosphorus concentrations were similarly assessed at the discretion of the attending clinician using the previously mentioned[d] chemistry analyzer or a point-of-care chemistry analyzer.[e] The lowest BG and lowest serum potassium, magnesium, and phosphorus concentrations measured during hospitalization were recorded. Time to resolution of DK/DKA status after initiation of short-acting insulin was recorded as the earliest time at which urine test strips showed no KBs.

Insulin was administered separately from intravenous fluids for those patients receiving short-acting insulin CRIs. Insulin CRIs were formulated as previously described,[13] and sliding scales were used based on serial BG measurement with CRI rates adjusted and dextrose supplemented accordingly. The ranges for BGs in these sliding scales were at the discretion of the attending clinician.

Outcome measures recorded included time to resolution of DK/DKA status from the time of initiation of short-acting insulin administration and length of hospitalization. Animals that were euthanized or were transferred to their primary veterinarians for continued care were so noted. These cases were included in assessment of complication rates if bloodwork was rechecked after initiation of short-acting insulin therapy prior to euthanasia or transfer, but were excluded from assessment of time to resolution of DK/DKA and length of hospitalization. Complications recorded included the development or worsening of hypokalemia, hypophosphatemia, or hypomagnesemia; hypoglycemia; and the presence of declining mentation or seizures. Laboratory values defining these complications are listed in Table 1.

Patients were divided into 2 groups based on time from admission until institution of short-acting insulin administration. Patients receiving short-acting insulin $\leq$6 hours after admission were assigned to the early group, and those receiving short-acting insulin >6 hours after admission were assigned to the late group. The groups were compared for differences in each of the outcome measures as well as rates of complications as described above. The association between severity of ketonuria at admission and time to resolution of DK/DKA was also evaluated.

Statistical methods

All data were tested for normality using the Kolmogorov–Smirnov test. Normally distributed continuous data are expressed as mean $\pm$ standard deviation and were compared between groups using the independent samples *t*-test, while nonnormally distributed data are expressed as median and range and were compared using the Mann–Whitney *U*-test. Proportions were compared between groups using Fisher's exact test or the chi-square test when more than 2 groups were compared. Time to resolution of DK/DKA, length of hospitalization, and baseline characteristics (age, rectal temperature, blood pressure, intake BG, and base excess) were compared between the early- and late-insulin administration groups. Proportions of patients experiencing each type of complication (eg, hypokalemia, hypophosphatemia, hypomagnesemia, hypoglycemia, declining mentation, or seizures) were compared between the early and late groups.

An ANOVA was used to assess whether more severe ketonuria was associated with slower resolution of DK/DKA status. To assess the effect of more severe degrees of acidemia on the resolution of DK/DKA, a backward stepwise multiple linear regression analysis was performed with variables retained if $P < 0.05$ (the model included pH at admission and early- vs. late-insulin therapy). All analyses were performed using commercial statistical software.[f] Significance was set at $P < 0.05$.

Results

Ninety medical records comprising 112 total cases for treatment of DK/DKA were identified. The following cases were excluded from analysis: 27 cases that were euthanized on presentation, 6 that were discharged against medical advice (1 that was later represented and euthanized, included above), 6 that were documented to be DK/DKA on the basis of KB measured in serum only, 6 that were started on long-acting insulin prior to the resolution of DK/DKA, 2 that had medical records missing, 2 that had short-acting insulin administered at unclear times, 1 that died prior to therapy, 1 that transferred to the primary veterinarian prior to initiation of short-acting insulin therapy, and 1 that was treated with long-acting insulin only.

Sixty cases remained, representing 49 individual patients. Of these, 37 were dogs (75.5%) and 12 were cats (24.5%). Overall, 44 cases were included in the early insulin therapy group with a median of 4 hours to initiation of short-acting insulin (range 0–6 h) and 16 cases were included in the late-insulin therapy group a median of 8.25 hours to initiation of short-acting insulin (range 7–21 h). Table 2 summarizes the baseline characteristics examined. There were no statistically significant differences in any of the baseline characteristics examined between the early- and late-insulin therapy groups.

Eight cases were euthanized, 7 (16%) in the early insulin group and 1 (6.3%) in the late-insulin group,

Table 1: Summary of blood values used when assessing for hypokalemia, hypophosphatemia, hypomagnesemia, and hypoglycemia

		Canine values	Feline values
Hypokalemia	Laboratory Blood Chemistry Analyzer‡	<3.8 mmol/L [3.8 mEq/L]	<3.8 mmol/L [3.8 mEq/L]
	Blood Gas Analyzer*	<3.9 mmol/L [3.9 mEq/L]	<3.3 mmol/L [3.3 mEq/L]
Hypophosphatemia	Laboratory Blood Chemistry Analyzer‡	<0.9 mmol/L [2.9 mg/dL]	<0.9 mmol/L [2.9 mg/dL]
	Point-of-Care Blood Chemistry Analyzer§	<0.8 mmol/L [2.5 mg/dL]	<1 mmol/L [3.1 mg/dL]
Hypomagnesemia	Laboratory Blood Chemistry Analyzer‡	<0.7 mmol/L [1.4 mEq/L]	<0.7 mmol/L [1.4 mEq/L]
	Point-of-Care Blood Chemistry Analyzer§	<0.7 mmol/L [1.4 mEq/L]	<0.75 mmol/L [1.5 mEq/L]
Hypoglycemia	Blood Gas Analyzer* and Glucometer†	<3.3 mmol/L [60 mg/dL]	<3.5 mmol/L [63 mg/dL]

*Siemens Rapidpoint 405, Deerfield, IL.
†Arkray Assure 4, Edina, MN.
‡Chemistry analyzer, Hitachi, Modular P, Dallas, TX.
§IDEXX VetTest 8008, Westbrook, ME.

Table 2: Summary of baseline characteristics recorded at hospital admission in animals administered short-acting insulin within 6 hours of admission (early) versus more than 6 hours after admission (late)

		Early	Late	*P*-value
Number of dog visits		34 (73.9%)	12 (26.1%)	
Age		9.0 (2.0–15.0)	8.0 (3.0–13.0)	0.401‡
Sex	Spayed	16/34 (47.0%)	6/12 (50.0%)	1.000*
	Castrated	14/34 (41.2%)	6 /12(50.0%)	0.738*
	Female	2/34 (5.9%)	0	1.000*
	Male	2/34 (5.9%)	0	1.000*
Number of cat visits		10 (71.4%)	4 (28.6%)	
Age		10.5 (2.0–20.0)	9.0 (2.0–15.0)	0.888‡
Sex	Spayed	3/10 (30%)	1/4 (25%)	1.000*
	Castrated	7/10 (70%)	3/4 (75%)	1.000*
	Female	0	0	–
	Male	0	0	–
Hypothermia		9/44 (20.5%)	5/16 (31.3%)	0.492*
Hypotension		2/32 (6.3%)	0/14 (0%)	1.000*
Blood glucose		27.3 ± 9.3 mmol/L (490 ± 167 mg/dL)	24.6 ± 11 mmol/L (444 ± 198 mg/dL)	0.370†
Base excess		−12.4 ± 8.5 mmol/L	−14.7 ± 7.1 mmol/L	0.350†
Degree of ketonuria	Mild	7/42 (16.7%)	3/16 (18.8%)	0.889§
	Moderate	6/42 (14.3%)	3/16 (18.8%)	
	Severe	29/42 (69.0%)	10/16 (62.5%)	
Previous diagnosis of diabetes mellitus		21/44 (47.7%)	9/16 (56.3%)	0.771*
Route of insulin	CRI	30/44 (68.2%)	7/16 (43.8%)	0.196§
	IM	12/44 (27.3%)	7/16 (43.8%)	
	SQ	2/44 (4.5%)	2/16 (12.5%)	

Normally distributed data are expressed as mean ± standard deviation, and nonnormally distributed data are expressed as median (range). Proportions are expressed with the total number of animals for which baseline data were available in the denominator and the percentage in parentheses.
†Normally distributed data were compared with independent samples t-tests.
‡Nonnormally distributed data were compared with Mann–Whitney *U*-tests.
∗Proportions were compared with the Fisher's exact test.
§Proportions with more than 2 categories were compared with the chi-square test. CRI, continuous rate infusion.

and 2 cases (both in the early group) transferred to their primary care veterinarian after initiation of short-acting insulin therapy, but prior to resolution of DK/DKA status. These cases were included in the assessment of treatment complications if bloodwork was reassessed, but were not included in analysis of time to resolution of DK/DKA status or length of hospitalization.

Ketonuria resolved more rapidly in the early insulin therapy group (Figure 1) (Table 3). Ketonuria also resolved more rapidly in cases with less severe ketonuria at presentation than in cases with more severe ketonuria on presentation (Figure 2) (Table 3).

Multiple linear regression analysis showed that of pH and early- versus late-insulin therapy, only early- versus late-insulin therapy was associated with time to resolution of DK/DKA status (coefficient = 19.0, 95% confidence interval 4.0–34.0, $P = 0.014$), suggesting that on average, resolution of DK/DKA status occurred

Table 3: Summary of resolution of ketonuria in the early- versus late-insulin administration groups and in those animals with mild, moderate, and severe degrees of ketonuria

		Resolution of ketonuria (h)	*P*-value
Time to short-acting insulin	Early ($n = 33$)	36.4 ± 22.6	0.014
	Late ($n = 15$)	55.4 ± 26.6	
Degree of ketonuria	Mild ($n = 8$)	23.4 ± 21.9	0.005 all individual pairwise $P < 0.05$
	Moderate ($n = 8$)	29.6 ± 19	
	Severe ($n = 31$)	50.9 ± 24.2	

Values for resolution of ketonuria are presented as a mean ± standard deviation.

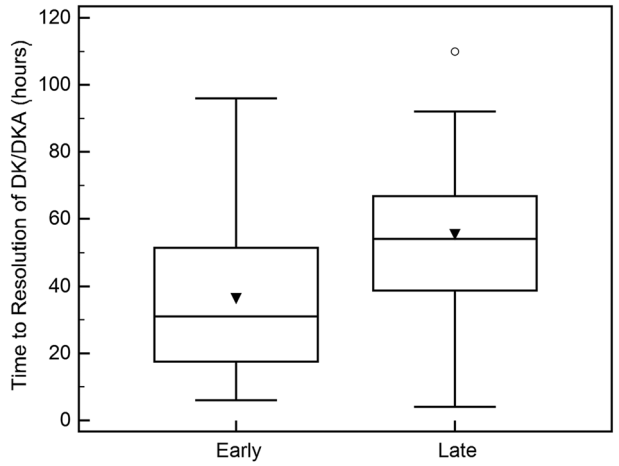

Figure 1: Box and whisker plots of the time to resolution of DK/DKA (h) after institution of short-acting insulin therapy in the early ($n = 33$) and late ($n = 15$) insulin therapy groups. The mean for each group is denoted by the black triangle. The lower and upper margins of the larger box for each group represent the lower and upper quartiles. The median for each group is represented by the middle line. The lower and upper horizontal lines extending off of the central box represent the minimum and maximum data points for each group. The single outlier representing greater than 1.5× the interquartile range from the median is represented as an open circle. DK, diabetic ketosis; DKA, diabetic ketoacidosis.

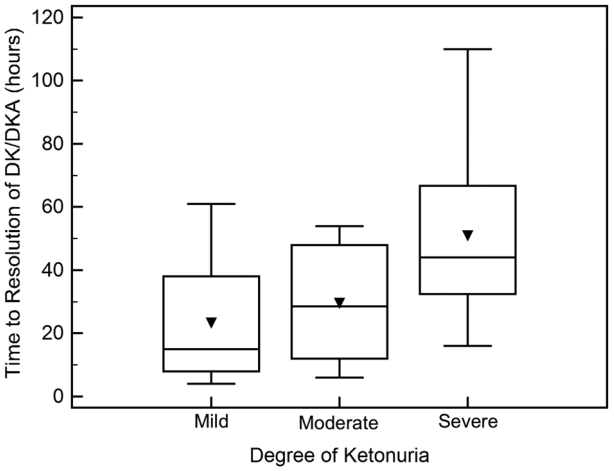

Figure 2: Box and whisker plots of the time to resolution of DK/DKA (h) for animals with mild ($n = 8$), moderate ($n = 8$), or severe ($n = 31$) ketonuria at admission. The mean for each group is denoted by the black triangle. The lower and upper margins of the larger box for each group represent the lower and upper quartiles. The median for each group is represented by the middle line. The lower and upper horizontal lines extending off of the central box represent the minimum and maximum data points for each group. DK, diabetic ketosis; DKA, diabetic ketoacidosis.

Table 4: Summary of the incidence of hypokalemia, hypophosphatemia, hypomagnesemia, and hypoglycemia in the early- versus late-insulin administration groups

	Early	Late	*P*-value
Hypokalemia	10/44 (22.7%)	5/15 (33.3%)	0.254
Hypophosphatemia	12/42 (28.6%)	9/15 (60.0%)	0.059
Hypomagnesemia	10/39 (25.6%)	4/12 (33.3%)	0.715
Hypoglycemia	0/44 (0%)	1/15 (6.7%)	0.254

approximately 19 hours earlier in patients in the early-insulin group.

The incidences of hypokalemia, hypophosphatemia, hypomagnesemia, and hypoglycemia are summarized in Table 4. There were no differences in the incidence of complications between the early and late groups. Neurologic signs were not observed in any case.

Length of hospitalization was not associated with time of short-acting insulin administration. The average length of hospitalization in the early-insulin administration group was 4.9 ± 2.4 days, and in the late-insulin administration group 5.7 ± 2.2 days ($P = 0.135$).

Discussion

The present study documented that early administration of short-acting insulin was associated with more rapid resolution of DK/DKA without an increase in complication rates. To the authors' knowledge this is the first veterinary study evaluating the effects of timing of the initiation of short-acting insulin therapy in the DK/DKA patient.

Current guidelines in people recommend initiating insulin administration 1 hour after initiating intravenous fluid therapy.[21] To the authors' knowledge, while this is a widely accepted tenet in the management of DK/DKA, there have been no randomized studies evaluating the optimal timing for the initiation of short-acting insulin in people. There was, however, a nonrandomized study in people exploring the use of a standardized protocol in the treatment of DK/DKA. With this protocolized approach, insulin administration occurred earlier and more in line with current recommendations, and resulted in more rapid resolution of ketosis.[24] Our findings were similar, showing that earlier administration of insulin resulted in more rapid resolution of ketosis.

Insulin is required in the DK/DKA patient to halt ketogenesis and enhance KB metabolism.[13] Without insulin therapy, KB production continues, potentially leading to concentrations exceeding those documented on hospital admission. This provides a potential mechanism to explain our finding that earlier insulin therapy resolved DK/DKA more quickly than delayed management. Ketonuria at the time of admission to the hospital rather than at the time of institution of insulin therapy was assessed as the baseline value in this study. It is possible that urine ketone concentrations may have remained higher in the late group due to continued production in the absence of insulin therapy, thereby taking longer to resolve. Because urine ketone concentrations were measured at admission and were generally not measured at the time of initiation of insulin therapy, an analysis of this was not possible. It is also possible that urine ketone concentrations may have been lower by the time of insulin administration in the late group due to further dilution from fluid therapy.

Complication rates including electrolyte derangements, hypoglycemia, and neurologic changes were similar between animals in the early- and late-insulin administration groups. Much of the support proposed for delaying insulin therapy in DK/DKA patients stems from the belief that complications may occur with early-insulin administration. Based on our findings, delay of insulin administration was not associated with a protective effect, suggesting that avoidance of electrolyte, hypoglycemic, or neurologic complications may not provide a sound rationale for delaying insulin therapy.

Electrolyte derangements have been documented to occur frequently pretreatment and with implementation of fluid and insulin therapy in DK/DKA patients.[2,4,5,9,19,25,26] The mechanism of hypokalemia, hypophosphatemia, and hypomagnesemia due to insulin therapy should be independent of the timing of insulin administration, though derangements may be less likely or less severe in patients receiving supplementation for a longer period before starting insulin. All hypokalemic or normokalemic patients received supplemental potassium immediately after initial volume resuscitation, and phosphorous and magnesium were monitored at least daily and supplemented as needed. Therefore, it is not surprising that the incidence of electrolyte derangements was similar between the early- and late-insulin groups in this study. This finding is similar to the study by Claus et al comparing different insulin infusions in cats with DK/DKA, which showed no differences in electrolyte derangements between treatment groups.[3] However, the findings in both studies should be interpreted cautiously, as electrolyte derangements may have gone undetected in patients with less frequent electrolyte monitoring.

Similar to the Claus et al study,[3] hypoglycemia only occurred in 1 patient in the late-insulin administration group during treatment for DK/DKA in the present study. Hypoglycemia can occur secondary to insulin therapy, but due to the serial monitoring of BG and dextrose supplementation protocols based on the sliding scales available for the treatment of DK/DKA, it occurs infrequently.

Perhaps the greatest concern during treatment of DK/DKA in the past has been the development of CE. Hyperosmolality can accompany DK/DKA, and should be normalized gradually. It has generally been recommended to delay insulin administration until after initial volume expansion and initiation of rehydration.[27] Recent studies in veterinary medicine have demonstrated that despite significant decreases in BG concentrations with conventional therapy, serum tonicity or effective osmolality remains relatively unchanged due to increases in serum sodium concentration, because sodium is the major determinant of serum tonicity.[17,18] This minimal change represents a likely reason for the low incidence of osmotic-mediated neurologic complications during the treatment of DK/DKA in general,[9] and the absence of more complications in the early-insulin administration group.

Our finding that earlier administration of short-acting insulin was not associated with a shorter length of hospitalization was unexpected. This differed from the findings of Bull et al, who documented shorter lengths of hospitalization with a protocolized approach including earlier administration of short-acting insulin in the management of DKA in people.[24] Patients presented for DK/DKA typically have comorbid conditions. Secondary or concurrent diseases contribute to the severity of DK/DKA due to increases in counterregulatory hormone concentrations.[2] Concurrent disorders were diagnosed in 69% of dogs with DKA in the study by Hume et al[5] and 93% of cats with DK/DKA in the study by Bruskiewicz et al.[4] It is likely that treatment for comorbid conditions contributed to length of hospitalization, potentially explaining the similarity in length of hospitalization between treatment groups. Because of the

retrospective nature of this study, it was not possible to determine the effect of treatment for comorbid conditions on length of hospitalization.

This study has several limitations. It is a retrospective study of a small patient population. There was no standardization for case allocation to the early- versus late-insulin administration group based on baseline characteristics, severity of illness measures, baseline hydration status, or preliminary clinical data. Additionally, there was no predetermined protocol for insulin administration or for the monitoring of complications. Due to equal representation in early- and late-insulin therapy groups, all cases were included in the analysis regardless of route of insulin administration. Monitoring for detection of DK/DKA resolution also was not standardized. Testing was performed on urine when animals voided if an indwelling urinary catheter was not in place. Unfortunately, even when animals voided urine, ketone measurements were not always performed.

In assessing for the resolution of DK/DKA it also would have been advantageous to assess serum KBs (including beta-hydroxybutyrate assessment) in conjunction with urinary KBs. However, assessment was not uniformly performed, limiting our ability to include this information in the present study. Due to differences in types of KBs detected by different methodologies and the normal metabolism of KBs, it has been recommended that beta-hydroxybutyrate monitoring replace urinary monitoring in people with DK/DKA.[27] There is also support in the veterinary literature for this practice.[28] It is therefore possible that our assessment of KB resolution was inaccurate in some cases.

It is worth noting that each case visit for patients that presented multiple times was included as an individual data point. This could potentially bias the results of the study if the attending clinician started insulin therapy in a similar time frame in the same patient at each admission.

In conclusion, early administration of insulin therapy in patients with DK/DKA is associated with a more rapid resolution of DK/DKA without a significant difference in complication rates. Although this did not lead to a reduction in the length of hospitalization, more rapid resolution of metabolic derangements is desirable, and our data support early initiation of insulin therapy. Future prospective studies are needed to assess the optimal timing of insulin administration in the treatment of critically ill diabetic patients.

Footnotes

[a] Siemens Rapidpoint 405, Deerfield, IL.
[b] Siemens Multistix 10 SG, Malvern, PA.
[c] Arkray Assure 4, Edina, MN.
[d] Chemistry analyzer, Hitachi, Modular P, Dallas, TX.
[e] IDEXX VetTest 8008, Westbrook, ME.
[f] MedCalc for Windows, version 9.5.0.0, MedCalc Software, Mariakerke, Belgium.

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